

10/550,099  
2nd

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NEWS 3 AUG 09 INSPEC enhanced with 1898-1968 archive  
NEWS 4 AUG 28 ADISCTI Reloaded and Enhanced  
NEWS 5 AUG 30 CA(SM)/Caplus(SM) Austrian patent law changes  
NEWS 6 SEP 11 CA/Caplus enhanced with more pre-1907 records  
NEWS 7 SEP 21 CA/Caplus fields enhanced with simultaneous left and right  
truncation  
NEWS 8 SEP 25 CA(SM)/Caplus(SM) display of CA Lexicon enhanced  
NEWS 9 SEP 25 CAS REGISTRY(SM) no longer includes Concord 3D coordinates  
NEWS 10 SEP 25 CAS REGISTRY(SM) updated with amino acid codes for pyrrolysine  
NEWS 11 SEP 28 CEABA-VTB classification code fields reloaded with new  
classification scheme  
NEWS 12 OCT 19 LOGOFF HOLD duration extended to 120 minutes  
NEWS 13 OCT 19 E-mail format enhanced  
NEWS 14 OCT 23 Option to turn off MARPAT highlighting enhancements available  
NEWS 15 OCT 23 CAS Registry Number crossover limit increased to 300,000 in  
multiple databases  
NEWS 16 OCT 23 The Derwent World Patents Index suite of databases on STN  
has been enhanced and reloaded  
NEWS 17 OCT 30 CHEMLIST enhanced with new search and display field  
NEWS 18 NOV 03 JAPIO enhanced with IPC 8 features and functionality  
NEWS 19 NOV 10 CA/Caplus F-Term thesaurus enhanced  
NEWS 20 NOV 10 STN Express with Discover! free maintenance release Version  
8.01c now available  
NEWS 21 NOV 13 CA/Caplus pre-1967 chemical substance index entries enhanced  
with preparation role  
NEWS 22 NOV 20 CAS Registry Number crossover limit increased to 300,000 in  
additional databases  
NEWS 23 NOV 20 CA/Caplus to MARPAT accession number crossover limit increased  
to 50,000  
NEWS 24 NOV 20 CA/Caplus patent kind codes will be updated  
NEWS 25 DEC 01 CAS REGISTRY updated with new ambiguity codes  
NEWS 26 DEC 11 CAS REGISTRY chemical nomenclature enhanced

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT  
MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),  
AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

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=>

Uploading

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Do you want to switch to the Registry File?

Choice (Y/n):

Switching to the Registry File...

Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> FILE REGISTRY

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

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DICTIONARY FILE UPDATES: 13 DEC 2006 HIGHEST RN 915360-23-5

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<http://www.cas.org/ONLINE/UG/regprops.html>

=>

Uploading C:\Program Files\Stnexp\Queries\10550099a.str

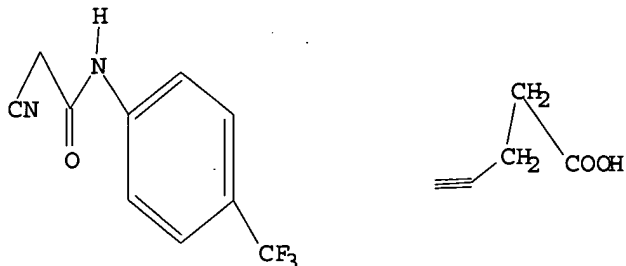
Print selected from Online session

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1

SAMPLE SEARCH INITIATED 09:27:55 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 0 TO ITERATE

100.0% PROCESSED 0 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 0 TO 0

PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1 sss full

FULL SEARCH INITIATED 09:28:02 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 1 TO ITERATE

100.0% PROCESSED 1 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

L3 0 SEA SSS FUL L1

=> file cas react

'CAS' IS AN AMBIGUOUS FILE OR CLUSTER NAME

CASLINK - Linked CAS files (Predefined Search Sequences)

CASRNS - CAS Registry Numbers Cluster

CA - The Chemical Abstracts File 1907-present

CASREACT - The Chemical Abstracts Reaction Search Service

ENTER FILE OR CLUSTER NAME (IGNORE):end

=>

Uploading C:\Program Files\Stnexp\Queries\10550099b.str

L4 STRUCTURE UPLOADED

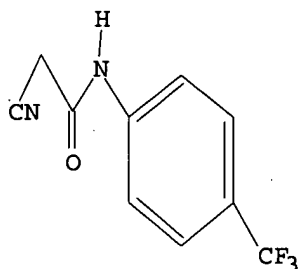
=> d l4

L4 HAS NO ANSWERS

Print selected from Online session

L4

STR



Structure attributes must be viewed using STN Express query preparation.

=> s l4

SAMPLE SEARCH INITIATED 09:29:32 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 51 TO ITERATE

100.0% PROCESSED 51 ITERATIONS

10 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 592 TO 1448

PROJECTED ANSWERS: 11 TO 389

L5 10 SEA SSS SAM L4

=> s l4 sss full

FULL SEARCH INITIATED 09:29:40 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 1184 TO ITERATE

100.0% PROCESSED 1184 ITERATIONS

SEARCH TIME: 00.00.01

259 ANSWERS

~~L6~~ 259 SEA SSS FUL L4

=>

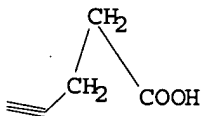
Uploading C:\Program Files\Stnexp\Queries\10550099c.str

L7 STRUCTURE UPLOADED

=> d l7

L7 HAS NO ANSWERS

L7 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l7

Print selected from Online session

SAMPLE SEARCH INITIATED 09:31:53 FILE 'REGISTRY'  
SAMPLE SCREEN SEARCH COMPLETED - 462 TO ITERATE

100.0% PROCESSED 462 ITERATIONS 17 ANSWERS  
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*  
PROJECTED ITERATIONS: 7951 TO 10529  
PROJECTED ANSWERS: 93 TO 587

L8 17 SEA SSS SAM L7

=> s l7 sss full  
FULL SEARCH INITIATED 09:31:59 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED - 8699 TO ITERATE

100.0% PROCESSED 8699 ITERATIONS  
SEARCH TIME: 00.00.01

408 ANSWERS

L9 408 SEA SSS FUL L7

=> file hcaplus  
COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
503.02	503.23

FULL ESTIMATED COST

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FILE COVERS 1907 - 14 Dec 2006 VOL 145 ISS 25  
FILE LAST UPDATED: 13 Dec 2006 (20061213/ED)

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=> d his

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L1 STRUCTURE UPLOADED  
L2 0 S L1  
L3 0 S L1 SSS FULL

Print selected from Online session

L4 STRUCTURE UPLOADED  
L5 10 S L4  
L6 259 S L4 SSS FULL  
L7 STRUCTURE UPLOADED  
L8 17 S L7  
L9 408 S L7 SSS FULL

FILE 'HCAPLUS' ENTERED AT 09:32:19 ON 14 DEC 2006

=> s l6  
L10 321 L6

=> s l9  
L11 720 L9

=> s l10 and l11  
L12 2 L10 AND L11

=> d l12 ibib abs hitstr tot

L12 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 2005:1004780 HCAPLUS  
DOCUMENT NUMBER: 143:284722  
TITLE: Anti-FK778 antibodies and highly sensitive immunoassay  
INVENTOR(S): Tamura, Kouichi; Kato, Takeshi; Tabata, Kenji  
PATENT ASSIGNEE(S): Astellas Pharma Inc., Japan  
SOURCE: PCT Int. Appl., 45 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

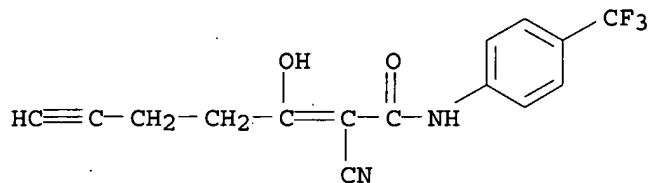
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005085290	A1	20050915	WO 2005-JP3819	20050228
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, GU, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2558596	AA	20050915	CA 2005-2558596	20050228
EP 1723179	A1	20061122	EP 2005-720091	20050228
R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR			
PRIORITY APPLN. INFO.:			AU 2004-901191	A 20040305
			WO 2005-JP3819	W 20050228
AB	The authors disclose the preparation of haptens for the elicitation of antibodies capable of binding to FK778. In addition, the authors disclose a highly-sensitive immunoassay method, which utilizes an antibody to the FK778, and a test kit for measuring the concentration of FK778.			
IT	185915-33-7, FK778			
RL:	ANT (Analyte); ANST (Analytical study)			

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(anti-FK778 antibodies and immunoassay)

RN 185915-33-7 HCAPLUS

CN 2-Hepten-6-ynamide, 2-cyano-3-hydroxy-N-[4-(trifluoromethyl)phenyl]- (9CI)  
(CA INDEX NAME)



IT 864381-46-4P, FR 266831

RL: BSU (Biological study, unclassified); SPN (Synthetic preparation);

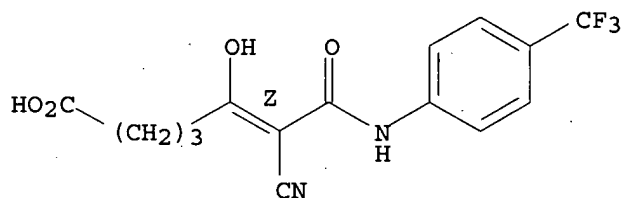
BIOL (Biological study); PREP (Preparation)

(preparation and carrier protein conjugation of)

RN 864381-46-4 HCAPLUS

CN 5-Heptenoic acid, 6-cyano-5-hydroxy-7-oxo-7-[[4-(trifluoromethyl)phenyl]amino]-, (5Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



IT 864378-17-6P

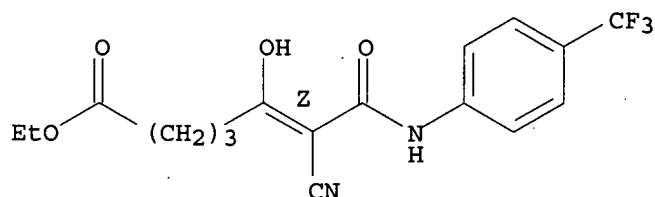
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)

(preparation and hydrolysis of)

RN 864378-17-6 HCAPLUS

CN 5-Heptenoic acid, 6-cyano-5-hydroxy-7-oxo-7-[[4-(trifluoromethyl)phenyl]amino]-, ethyl ester, (5Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



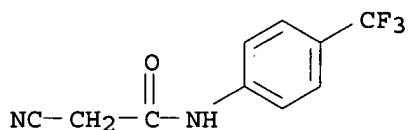
IT 24522-30-3P 864378-18-7P 864378-19-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)

(preparation of)

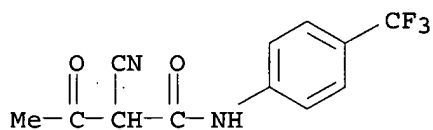
RN 24522-30-3 HCAPLUS

CN Acetamide, 2-cyano-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 864378-18-7 HCAPLUS

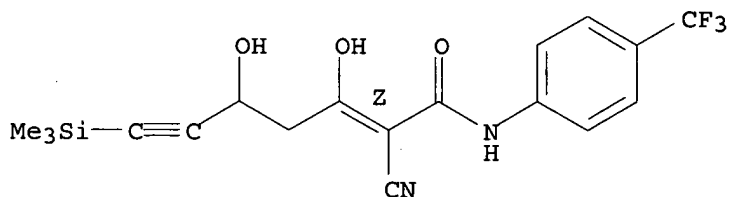
CN Butanamide, 2-cyano-3-oxo-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 864378-19-8 HCAPLUS

CN 2-Hepten-6-ynamide, 2-cyano-3,5-dihydroxy-N-[4-(trifluoromethyl)phenyl]-7-(trimethylsilyl)-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



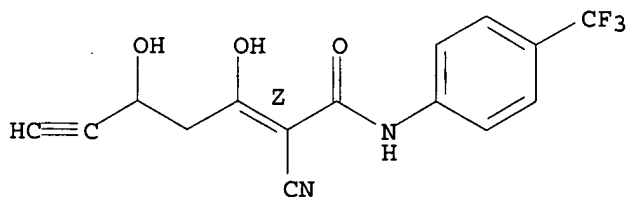
IT 864381-47-5P, FR 271764

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

RN 864381-47-5 HCAPLUS

CN 2-Hepten-6-ynamide, 2-cyano-3,5-dihydroxy-N-[4-(trifluoromethyl)phenyl]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



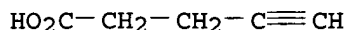
IT 6089-09-4, 4-Pentynoic acid

RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction with cyanoacetylaminophenoxy hexanoate)

RN 6089-09-4 HCAPLUS

CN 4-Pentynoic acid (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)





REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:817854 HCAPLUS

DOCUMENT NUMBER: 141:313895

TITLE: Process for preparation of 2-cyano-3-hydroxy-hept-2-en-6-ynoic acid N-(4-trifluoromethylphenyl) amide

INVENTOR(S): Omori, Hiroki; Kubota, Ariyoshi; Kawakami, Takeshi; Fujii, Yosuke; Matsumoto, Ikuo; Kitayama, Masato; Goto, Shunsuke; Hirabayashi, Satoshi

PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co. Ltd., Japan

SOURCE: PCT Int. Appl., 49 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004085383	A1	20041007	WO 2004-JP3904	20040323
W:	AE, AG, AL, AM, AN, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, GU, HK, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
EP 1609778	A1	20051228	EP 2004-722662	20040323
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK			
US 2006217440	A1	20060928	US 2005-550099	20050921
PRIORITY APPLN. INFO.:			JP 2003-81335	A 20030324
			JP 2003-176706	A 20030620
			WO 2004-JP3904	W 20040323

OTHER SOURCE(S): CASREACT 141:313895

AB This invention pertains to a method for producing 2-cyano-3-hydroxy-hept-2-en-6-ynoic acid N-(4-trifluoromethylphenyl) amide, which comprises reacting 4-trifluoromethylaniline with 4-pentynoic acid in acetone in the presence of K<sub>2</sub>CO<sub>3</sub> and iso-Pr chlorocarbonate. A-, B-, and C-form crystals of the title compound were each selectively produced by recrystn. under the conditions of controlled recrystn. temperature and/or controlled recrystn. (precipitation) time. This invention provides a method to make the title compound

in mild conditions without the production of industrial waste.

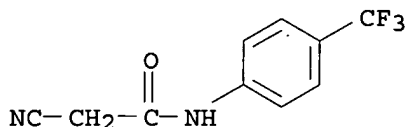
IT 24522-30-3P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

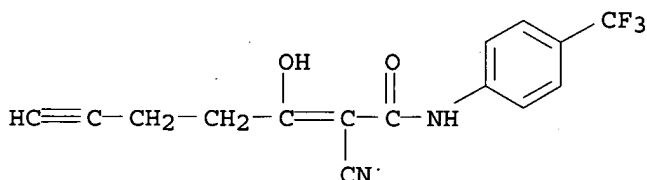
(intermediate; preparation of 2-cyano-3-hydroxy-hept-2-en-6-ynoic acid

Print selected from Online session

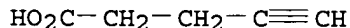
N-(4-trifluoromethylphenyl) amide)  
RN 24522-30-3 HCAPLUS  
CN Acetamide, 2-cyano-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



IT 185915-33-7P  
RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)  
(preparation of 2-cyano-3-hydroxy-hept-2-en-6-ynoic acid  
N-(4-trifluoromethylphenyl) amide)  
RN 185915-33-7 HCAPLUS  
CN 2-Hepten-6-ynamide, 2-cyano-3-hydroxy-N-[4-(trifluoromethyl)phenyl]- (9CI)  
(CA INDEX NAME)



IT 6089-09-4, 4-Pentynoic acid  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation of 2-cyano-3-hydroxy-hept-2-en-6-ynoic acid  
N-(4-trifluoromethylphenyl) amide)  
RN 6089-09-4 HCAPLUS  
CN 4-Pentynoic acid (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> FIL REGISTRY

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
30.46	533.69

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
-1.50	-1.50

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DICTIONARY FILE UPDATES: 13 DEC 2006 HIGHEST RN 915360-23-5

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<http://www.cas.org/ONLINE/UG/regprops.html>

=>

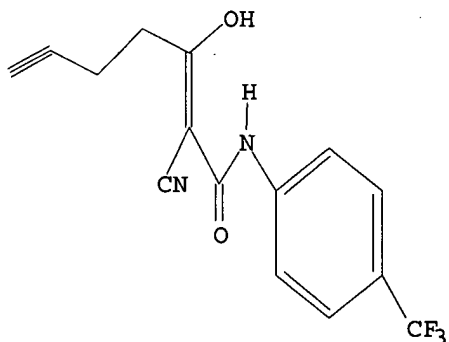
Uploading C:\Program Files\Stnexp\Queries\10550099d.str

L13 STRUCTURE UPLOADED

=> d l13

L13 HAS NO ANSWERS

L13 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l13

SAMPLE SEARCH INITIATED 09:37:32 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 0 TO ITERATE

100.0% PROCESSED 0 ITERATIONS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 0 TO 0

PROJECTED ANSWERS: 0 TO 0

0 ANSWERS

Print selected from Online session

L14 0 SEA SSS SAM L13

=> s l13 sss full

FULL SEARCH INITIATED 09:37:38 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 15 TO ITERATE

100.0% PROCESSED 15 ITERATIONS

SEARCH TIME: 00.00.01

9 ANSWERS

L15 9 SEA SSS FUL L13

=> FIL HCAPLUS

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

166.94

700.63

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

0.00

-1.50

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FILE COVERS 1907 - 14 Dec 2006 VOL 145 ISS 25

FILE LAST UPDATED: 13 Dec 2006 (20061213/ED)

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=> s l15

L16 109 L15

=> d his

(FILE 'HOME' ENTERED AT 09:27:21 ON 14 DEC 2006)

FILE 'REGISTRY' ENTERED AT 09:27:41 ON 14 DEC 2006

L1 STRUCTURE UPLOADED

L2 0 S L1

L3 0 S L1 SSS FULL

L4 STRUCTURE UPLOADED

L5 10 S L4

L6 259 S L4 SSS FULL

L7 STRUCTURE UPLOADED

Print selected from Online session

L8 17 S L7  
L9 408 S L7 SSS FULL

FILE 'HCAPLUS' ENTERED AT 09:32:19 ON 14 DEC 2006

L10 321 S L6  
L11 720 S L9  
L12 2 S L10 AND L11

FILE 'REGISTRY' ENTERED AT 09:37:14 ON 14 DEC 2006

L13 STRUCTURE UPLOADED  
L14 0 S L13  
L15 9 S L13 SSS FULL

FILE 'HCAPLUS' ENTERED AT 09:37:43 ON 14 DEC 2006

L16 109 S L15

=> s l6 and l16

321 L6  
L17 109 L6 AND L16

=> s l9 and l16

720 L9  
L18 2 L9 AND L16

=> d l18 ibib abs hitstr tot

L18 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1004780 HCAPLUS

DOCUMENT NUMBER: 143:284722

TITLE: Anti-FK778 antibodies and highly sensitive immunoassay

INVENTOR(S): Tamura, Kouichi; Kato, Takeshi; Tabata, Kenji

PATENT ASSIGNEE(S): Astellas Pharma Inc., Japan

SOURCE: PCT Int. Appl., 45 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005085290	A1	20050915	WO 2005-JP3819	20050228
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2558596	AA	20050915	CA 2005-2558596	20050228
EP 1723179	A1	20061122	EP 2005-720091	20050228
R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR			
PRIORITY APPLN. INFO.:			AU 2004-901191	A 20040305
			WO 2005-JP3819	W 20050228

Print selected from Online session

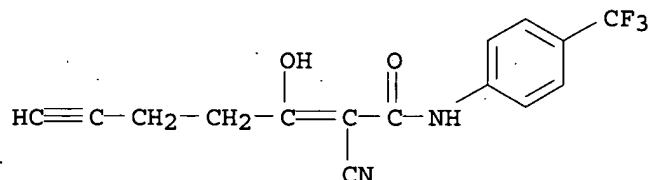
AB The authors disclose the preparation of haptens for the elicitation of antibodies capable of binding to FK778. In addition, the authors disclose a highly-sensitive immunoassay method, which utilizes an antibody to the FK778, and a test kit for measuring the concentration of FK778.

IT 185915-33-7, FK778

RL: ANT (Analyte); ANST (Analytical study)  
(anti-FK778 antibodies and immunoassay)

RN 185915-33-7 HCAPLUS

CN 2-Hepten-6-ynamide, 2-cyano-3-hydroxy-N-[4-(trifluoromethyl)phenyl]- (9CI)  
(CA INDEX NAME)

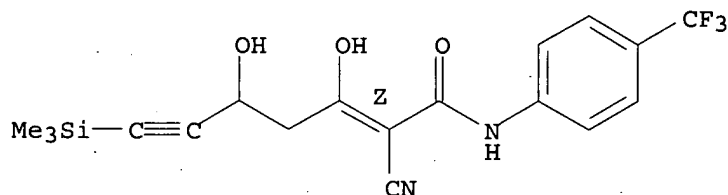


IT 864378-19-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation of)

RN 864378-19-8 HCAPLUS

CN 2-Hepten-6-ynamide, 2-cyano-3,5-dihydroxy-N-[4-(trifluoromethyl)phenyl]-7-(trimethylsilyl)-, (2Z)- (9CI) (CA INDEX NAME)



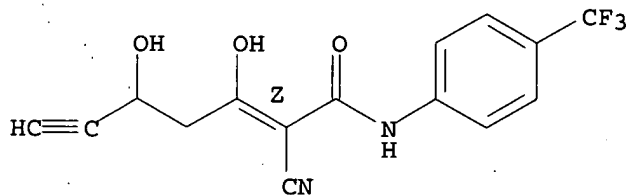
IT 864381-47-5P, FR 271764

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

RN 864381-47-5 HCAPLUS

CN 2-Hepten-6-ynamide, 2-cyano-3,5-dihydroxy-N-[4-(trifluoromethyl)phenyl]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



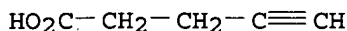
IT 6089-09-4, 4-Pentynoic acid

Print selected from Online session

RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction with cyanoacetylaminophenoxy hexanoate)

RN 6089-09-4 HCAPLUS

CN 4-Pentynoic acid (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:817854 HCAPLUS

DOCUMENT NUMBER: 141:313895

TITLE: Process for preparation of 2-cyano-3-hydroxy-hept-2-en-6-ynoic acid N-(4-trifluoromethylphenyl) amide

INVENTOR(S): Omori, Hiroki; Kubota, Ariyoshi; Kawakami, Takeshi; Fujii, Yosuke; Matsumoto, Ikuo; Kitayama, Masato; Goto, Shunsuke; Hirabayashi, Satoshi

PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co. Ltd., Japan

SOURCE: PCT Int. Appl., 49 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004085383	A1	20041007	WO 2004-JP3904	20040323
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1609778	A1	20051228	EP 2004-722662	20040323
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
US 2006217440	A1	20060928	US 2005-550099	20050921
PRIORITY APPLN. INFO.:			JP 2003-81335	A 20030324
			JP 2003-176706	A 20030620
			WO 2004-JP3904	W 20040323

OTHER SOURCE(S): CASREACT 141:313895

AB This invention pertains to a method for producing 2-cyano-3-hydroxy-hept-2-en-6-ynoic acid N-(4-trifluoromethylphenyl) amide, which comprises reacting 4-trifluoromethylaniline with 4-pentynoic acid in acetone in the presence of K<sub>2</sub>CO<sub>3</sub> and iso-Pr chlorocarbonate. A-, B-, and C-form crystals of the title compound were each selectively produced by recrystn. under the conditions of controlled recrystn. temperature and/or controlled recrystn. (precipitation) time. This invention provides a method to make the title compound

in mild conditions without the production of industrial waste.

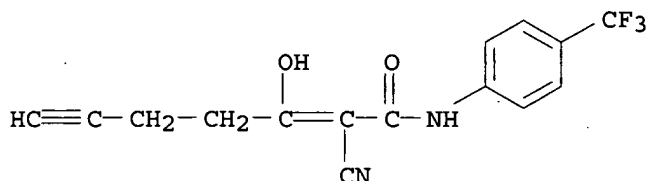
Print selected from Online session

IT 185915-33-7P

RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)  
(preparation of 2-cyano-3-hydroxy-hept-2-en-6-ynoic acid  
N-(4-trifluoromethylphenyl) amide)

RN 185915-33-7 HCAPLUS

CN 2-Hepten-6-ynamide, 2-cyano-3-hydroxy-N-[4-(trifluoromethyl)phenyl]- (9CI)  
(CA INDEX NAME)

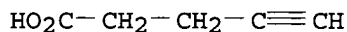


IT 6089-09-4, 4-Pentynoic acid

RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation of 2-cyano-3-hydroxy-hept-2-en-6-ynoic acid  
N-(4-trifluoromethylphenyl) amide)

RN 6089-09-4 HCAPLUS

CN 4-Pentynoic acid (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



REFERENCE COUNT:

7

THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT



10550099.trn

*WAT*

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PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS 3 AUG 09 INSPEC enhanced with 1898-1968 archive  
NEWS 4 AUG 28 ADISCTI Reloaded and Enhanced  
NEWS 5 AUG 30 CA(SM)/CAplus(SM) Austrian patent law changes  
NEWS 6 SEP 11 CA/CAplus enhanced with more pre-1907 records  
NEWS 7 SEP 21 CA/CAplus fields enhanced with simultaneous left and right  
truncation  
NEWS 8 SEP 25 CA(SM)/CAplus(SM) display of CA Lexicon enhanced  
NEWS 9 SEP 25 CAS REGISTRY(SM) no longer includes Concord 3D coordinates  
NEWS 10 SEP 25 CAS REGISTRY(SM) updated with amino acid codes for pyrrolysine  
NEWS 11 SEP 28 CEABA-VTB classification code fields reloaded with new  
classification scheme  
NEWS 12 OCT 19 LOGOFF HOLD duration extended to 120 minutes  
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NEWS 14 OCT 23 Option to turn off MARPAT highlighting enhancements available  
NEWS 15 OCT 23 CAS Registry Number crossover limit increased to 300,000 in  
multiple databases  
NEWS 16 OCT 23 The Derwent World Patents Index suite of databases on STN  
has been enhanced and reloaded  
NEWS 17 OCT 30 CHEMLIST enhanced with new search and display field  
NEWS 18 NOV 03 JAPIO enhanced with IPC 8 features and functionality  
NEWS 19 NOV 10 CA/CAplus F-Term thesaurus enhanced  
NEWS 20 NOV 10 STN Express with Discover! free maintenance release Version  
8.01c now available  
NEWS 21 NOV 13 CA/CAplus pre-1967 chemical substance index entries enhanced  
with preparation role  
  
NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT  
MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),  
AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.  
  
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FILE 'HOME' ENTERED AT 11:27:32 ON 19 NOV 2006

=>

Uploading

THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE

Do you want to switch to the Registry File?

Choice (Y/n):

Switching to the Registry File...

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=> FILE REGISTRY

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'REGISTRY' ENTERED AT 11:27:42 ON 19 NOV 2006

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STRUCTURE FILE UPDATES: 17 NOV 2006 HIGHEST RN 913607-70-2

DICTIONARY FILE UPDATES: 17 NOV 2006 HIGHEST RN 913607-70-2

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TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

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<http://www.cas.org/ONLINE/UG/regprops.html>

=>

Uploading C:\Program Files\Stnexp\Queries\10550099.str

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR

/ Structure 1 in file .gra /

Structure attributes must be viewed using STN Express query preparation.

10550099.trn

=> s l1

SAMPLE SEARCH INITIATED 11:27:56 FILE 'REGISTRY'  
SAMPLE SCREEN SEARCH COMPLETED - 51 TO ITERATE

100.0% PROCESSED 51 ITERATIONS 10 ANSWERS  
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*  
PROJECTED ITERATIONS: 592 TO 1448  
PROJECTED ANSWERS: 11 TO 389

L2 10 SEA SSS SAM L1

=> s l1 sss full

FULL SEARCH INITIATED 11:28:03 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED - 1178 TO ITERATE

100.0% PROCESSED 1178 ITERATIONS  
SEARCH TIME: 00.00.01

259 ANSWERS

L3 259 SEA SSS FUL L1

=>

Uploading C:\Program Files\Stnexp\Queries\10550099a.str

L4 STRUCTURE UPLOADED

=> d l4

L4 HAS NO ANSWERS

L4 STR

/ Structure 2 in file .gra /

Structure attributes must be viewed using STN Express query preparation.

=> s l4

SAMPLE SEARCH INITIATED 11:30:59 FILE 'REGISTRY'  
SAMPLE SCREEN SEARCH COMPLETED - 0 TO ITERATE

100.0% PROCESSED 0 ITERATIONS 0 ANSWERS  
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*  
PROJECTED ITERATIONS: 0 TO 0  
PROJECTED ANSWERS: 0 TO 0

L5 0 SEA SSS SAM L4

=> s l4 sss full

FULL SEARCH INITIATED 11:31:05 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED - 15 TO ITERATE

100.0% PROCESSED 15 ITERATIONS 9 ANSWERS  
SEARCH TIME: 00.00.01

10550099.trn

L6 9 SEA SSS FUL L4

=> FIL HCAPLUS

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

336.08

336.29

FILE 'HCAPLUS' ENTERED AT 11:31:43 ON 19 NOV 2006

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FILE COVERS 1907 - 19 Nov 2006 VOL 145 ISS 22

FILE LAST UPDATED: 17 Nov 2006 (20061117/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

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=> d his

(FILE 'HOME' ENTERED AT 11:27:32 ON 19 NOV 2006)

FILE 'REGISTRY' ENTERED AT 11:27:42 ON 19 NOV 2006

L1 STRUCTURE UPLOADED

L2 10 S L1

L3 259 S L1 SSS FULL

L4 STRUCTURE UPLOADED

L5 0 S L4

L6 9 S L4 SSS FULL

FILE 'HCAPLUS' ENTERED AT 11:31:43 ON 19 NOV 2006

=> s l3

L7 320 L3

=> s l6

L8 109 L6

=> s l7 and l8

L9 109 L7 AND L8

=> FIL REGISTRY

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

7.59

343.88

FILE 'REGISTRY' ENTERED AT 11:33:36 ON 19 NOV 2006

10550099.trn

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STRUCTURE FILE UPDATES: 17 NOV 2006 HIGHEST RN 913607-70-2  
DICTIONARY FILE UPDATES: 17 NOV 2006 HIGHEST RN 913607-70-2

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REGISTRY includes numerically searchable data for experimental and  
predicted properties as well as tags indicating availability of  
experimental property data in the original document. For information  
on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

=>

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L10 STRUCTURE UPLOADED

=> d l10

L10 HAS NO ANSWERS

L10 STR

/ Structure 3 in file .gra /

Structure attributes must be viewed using STN Express query preparation.

=> s l10

SAMPLE SEARCH INITIATED 11:33:53 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 460 TO ITERATE

100.0% PROCESSED 460 ITERATIONS

50 ANSWERS

INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 7914 TO 10486

PROJECTED ANSWERS: 1282 TO 2438

L11 50 SEA SSS SAM L10

=> s l10 sss full

FULL SEARCH INITIATED 11:34:01 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 8675 TO ITERATE

100.0% PROCESSED 8675 ITERATIONS

1787 ANSWERS

SEARCH TIME: 00.00.01

10550099.trn

L12 1787 SEA SSS FUL L10

=> FIL HCAPLUS

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

166.94

510.82

FILE 'HCAPLUS' ENTERED AT 11:34:08 ON 19 NOV 2006

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FILE COVERS 1907 - 19 Nov 2006 VOL 145 ISS 22

FILE LAST UPDATED: 17 Nov 2006 (20061117/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d his

(FILE 'HOME' ENTERED AT 11:27:32 ON 19 NOV 2006)

FILE 'REGISTRY' ENTERED AT 11:27:42 ON 19 NOV 2006

L1 STRUCTURE UPLOADED

L2 10 S L1

L3 259 S L1 SSS FULL

L4 STRUCTURE UPLOADED

L5 0 S L4

L6 9 S L4 SSS FULL

FILE 'HCAPLUS' ENTERED AT 11:31:43 ON 19 NOV 2006

L7 320 S L3

L8 109 S L6

L9 109 S L7 AND L8

FILE 'REGISTRY' ENTERED AT 11:33:36 ON 19 NOV 2006

L10 STRUCTURE UPLOADED

L11 50 S L10

L12 1787 S L10 SSS FULL

FILE 'HCAPLUS' ENTERED AT 11:34:08 ON 19 NOV 2006

=> s l12

L13 1504 L12

=> s l7 and l13

10550099.trn

L14 2 L7 AND L13

=> s 18 and process

2339339 PROCESS

1589446 PROCESSES

3492079 PROCESS

(PROCESS OR PROCESSES)

L15 10 L8 AND PROCESS

=> s 18 and l13

L16 2 L8 AND L13

=> d l14 ibib abs hitstr tot

L14 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1004780 HCAPLUS

DOCUMENT NUMBER: 143:284722

TITLE: Anti-FK778 antibodies and highly sensitive immunoassay

INVENTOR(S): Tamura, Kouichi; Kato, Takeshi; Tabata, Kenji

PATENT ASSIGNEE(S): Astellas Pharma Inc., Japan

SOURCE: PCT Int. Appl., 45 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005085290	A1	20050915	WO 2005-JP3819	20050228
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, VZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2558596	AA	20050915	CA 2005-2558596	20050228
PRIORITY APPLN. INFO.:			AU 2004-901191	A 20040305
			WO 2005-JP3819	W 20050228

AB The authors disclose the preparation of haptens for the elicitation of antibodies capable of binding to FK778. In addition, the authors disclose a highly-sensitive immunoassay method, which utilizes an antibody to the FK778, and a test kit for measuring the concentration of FK778.

IT 185915-33-7, FK778

RL: ANT (Analyte); ANST (Analytical study)  
(anti-FK778 antibodies and immunoassay)

RN 185915-33-7 HCAPLUS

CN 2-Hepten-6-ynamide, 2-cyano-3-hydroxy-N-[4-(trifluoromethyl)phenyl]- (9CI)  
(CA INDEX NAME)

/ Structure 4 in file .gra /

IT 864381-46-4P, FR 266831

RL: BSU (Biological study, unclassified); SPN (Synthetic preparation);

10550099.trn

BIOL (Biological study); PREP (Preparation)  
(preparation and carrier protein conjugation of)

RN 864381-46-4 HCAPLUS

CN 5-Heptenoic acid, 6-cyano-5-hydroxy-7-oxo-7-[[4-(trifluoromethyl)phenyl]amino]-, (5Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

/ Structure 5 in file .gra /

IT 864378-17-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and hydrolysis of)

RN 864378-17-6 HCAPLUS

CN 5-Heptenoic acid, 6-cyano-5-hydroxy-7-oxo-7-[[4-(trifluoromethyl)phenyl]amino]-, ethyl ester, (5Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

/ Structure 6 in file .gra /

IT 24522-30-3P 864378-18-7P 864378-19-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation of)

RN 24522-30-3 HCAPLUS

CN Acetamide, 2-cyano-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

/ Structure 7 in file .gra /

RN 864378-18-7 HCAPLUS

CN Butanamide, 2-cyano-3-oxo-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

/ Structure 8 in file .gra /

RN 864378-19-8 HCAPLUS

CN 2-Hepten-6-ynamide, 2-cyano-3,5-dihydroxy-N-[4-(trifluoromethyl)phenyl]-7-(trimethylsilyl)-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

/ Structure 9 in file .gra /

IT 864381-47-5P, FR 271764

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

RN 864381-47-5 HCAPLUS

CN 2-Hepten-6-ynamide, 2-cyano-3,5-dihydroxy-N-[4-(trifluoromethyl)phenyl]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

/ Structure 10 in file .gra /

IT 6089-09-4, 4-Pentynoic acid

RL: RCT (Reactant); RACT (Reactant or reagent)



(reaction with cyanoacetylaminophenoxy hexanoate)

RN 6089-09-4 HCAPLUS

CN 4-Pentynoic acid (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

/ Structure 11 in file .gra /

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:817854 HCAPLUS

DOCUMENT NUMBER: 141:313895

TITLE: Process for preparation of 2-cyano-3-hydroxy-hept-2-en-  
6-ynoic acid N-(4-trifluoromethylphenyl) amideINVENTOR(S): Omori, Hiroki; ~~Kubota~~, Ariyoshi; Kawakami, Takeshi;  
~~Fujii, Yosuke~~; Matsumoto, Ikuo; Kitayama, Masato;  
Goto, Shunsuke; Hirabayashi, Satoshi

PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co. Ltd., Japan

SOURCE: PCT Int. Appl., 49 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004085383	A1	20041007	WO 2004-JP3904	20040323
W: AE, AG, AL, AM, <del>AT</del> , AU, <del>AZ</del> , BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, <del>CZ</del> , <del>DE</del> , DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1609778	A1	20051228	EP 2004-722662	20040323
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
US 2006217440	A1	20060928	US 2005-550099	20050921
PRIORITY APPLN. INFO.:			JP 2003-81335	A 20030324
			JP 2003-176706	A 20030620
			WO 2004-JP3904	W 20040323

OTHER SOURCE(S): CASREACT 141:313895

AB This invention pertains to a method for producing 2-cyano-3-hydroxy-hept-2-en-6-ynoic acid N-(4-trifluoromethylphenyl) amide, which comprises reacting 4-trifluoromethylaniline with 4-pentynoic acid in acetone in the presence of K<sub>2</sub>CO<sub>3</sub> and iso-Pr chlorocarbonate. A-, B-, and C-form crystals of the title compound were each selectively produced by recrystn. under the conditions of controlled recrystn. temperature and/or controlled recrystn. (precipitation) time. This invention provides a method to make the title compound

in mild conditions without the production of industrial waste.

IT 24522-30-3P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

10550099.trn

(intermediate; preparation of 2-cyano-3-hydroxy-hept-2-en-6-ynoic acid  
N-(4-trifluoromethylphenyl) amide)

RN 24522-30-3 HCAPLUS

CN Acetamide, 2-cyano-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

/ Structure 12 in file .gra /

IT 185915-33-7P

RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic  
preparation); PREP (Preparation)

(preparation of 2-cyano-3-hydroxy-hept-2-en-6-ynoic acid  
N-(4-trifluoromethylphenyl) amide)

RN 185915-33-7 HCAPLUS

CN 2-Hepten-6-ynamide, 2-cyano-3-hydroxy-N-[4-(trifluoromethyl)phenyl]- (9CI)  
(CA INDEX NAME)

/ Structure 13 in file .gra /

IT 6089-09-4, 4-Pentynoic acid

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of 2-cyano-3-hydroxy-hept-2-en-6-ynoic acid  
N-(4-trifluoromethylphenyl) amide)

RN 6089-09-4 HCAPLUS

CN 4-Pentynoic acid (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

/ Structure 14 in file .gra /

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l15 ibib abs hitstr tot

L15 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:1090523 HCAPLUS

DOCUMENT NUMBER: 145:410662

TITLE: Pharmaceutical dosage forms and combination  
preparations of pyrimidine biosynthesis inhibitors for  
producing additional effects on the immune system

INVENTOR(S): Lindner, Juergen

PATENT ASSIGNEE(S): Germany

SOURCE: Ger. Offen., 22pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 102005017592	A1	20061019	DE 2005-102005017592	20050416
WO 2006111296	A2	20061026	WO 2006-EP3291	20060411
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG,			

SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN,  
YU, ZA, ZM, ZW  
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,  
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,  
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,  
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,  
KG, KZ, MD, RU, TJ, TM

## PRIORITY APPLN. INFO.:

DE 2005-102005017592A 20050416

AB The invention discloses a com. formulation of the pyrimidine biosynthesis inhibitor leflunomide for producing addnl. effects on the immune system. It was found that through pharmaceutical forms and/or combination prepsns. of pyrimidine biosynthesis inhibitors, which lead to daily multi-hour fluctuations of plasma concns. and/or to multi-hour daily fluctuations of pyrimidine biosynthesis inhibition, these pharmacodynamic actions on TH2-dependent processes and the development of e.g. regulatory immune responses can be achieved as such also with humans. Through these addnl. effects, these formulations are suitable to treat damaging immune reactions, e.g. autoimmune reactions or allergic reactions, as well as degenerative processes through the development of a regulatory immune response. A suitable pharmaceutical form represents e.g. quick-disintegrating hard gelatin capsules with a mixture of fine powdered leflunomide in glucose. A suitable combination preparation represents e.g. a combination with cholestyramine, which through a time-delayed effect (retarded release of cholestyramine) a few hours after resorption of leflunomide leads to a lowering of the blood plasma concentration of the effective metabolites of leflunomide.

IT 185915-33-7, MNA 715

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)

(pharmaceutical dosage forms and combination prepsns. of pyrimidine  
biosynthesis inhibitors for production of addnl. effects on immune system)

RN 185915-33-7 HCAPLUS

CN 2-Hepten-6-ynamide, 2-cyano-3-hydroxy-N-[4-(trifluoromethyl)phenyl]- (9CI)  
(CA INDEX NAME)

/ Structure 15 in file .gra /

L15 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:817854 HCAPLUS

DOCUMENT NUMBER: 141:313895

TITLE: Process for preparation of  
2-cyano-3-hydroxy-hept-2-en-6-ynoic acid  
N-(4-trifluoromethylphenyl) amide

INVENTOR(S): Omori, Hiroki; Kubota, Ariyoshi; Kawakami, Takeshi;  
Fujii, Yosuke; Matsumoto, Ikuo; Kitayama, Masato;  
Goto, Shunsuke; Hirabayashi, Satoshi

PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co. Ltd., Japan

SOURCE: PCT Int. Appl., 49 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004085383	A1	20041007	WO 2004-JP3904	20040323
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,			

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,  
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,  
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,  
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,  
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,  
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,  
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,  
SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,  
TD, TG

EP 1609778 A1 20051228 EP 2004-722662 20040323

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK

US 2006217440 A1 20060928 US 2005-550099 20050921

PRIORITY APPLN. INFO.: JP 2003-81335 A 20030324  
JP 2003-176706 A 20030620  
WO 2004-JP3904 W 20040323

OTHER SOURCE(S): CASREACT 141:313895

AB This invention pertains to a method for producing 2-cyano-3-hydroxy-hept-2-en-6-ynoic acid N-(4-trifluoromethylphenyl) amide, which comprises reacting 4-trifluoromethylaniline with 4-pentynoic acid in acetone in the presence of K<sub>2</sub>CO<sub>3</sub> and iso-Pr chlorocarbonate. A-, B-, and C-form crystals of the title compound were each selectively produced by recrystn. under the conditions of controlled recrystn. temperature and/or controlled recrystn. (precipitation) time. This invention provides a method to make the title compound

in mild conditions without the production of industrial waste.

IT 185915-33-7P

RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)  
(preparation of 2-cyano-3-hydroxy-hept-2-en-6-ynoic acid N-(4-trifluoromethylphenyl) amide)

RN 185915-33-7 HCAPLUS

CN 2-Hepten-6-ynamide, 2-cyano-3-hydroxy-N-[4-(trifluoromethyl)phenyl]- (9CI)  
(CA INDEX NAME)

/ Structure 16 in file .gra /

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:491810 HCAPLUS

DOCUMENT NUMBER: 141:98847

TITLE: New immunosuppressive strategies in renal transplant recipients

AUTHOR(S): Fischereder, Michael; Kretzler, Matthias

CORPORATE SOURCE: Nephrology Center, Medizinische Poliklinik Innenstadt, Ludwig-Maximilians University, Munich, Germany

SOURCE: Journal of Nephrology (2004), 17(1), 9-18

CODEN: JLNEEL; ISSN: 1121-8428

PUBLISHER: Wichtig Editore

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Along with expanded knowledge of pathophysiol. processes involved in transplant rejection, a variety of immunosuppressive agents with very specific modes of action have been developed. The focus of this review is an update on the pathophysiol. rationale and experience with such agents in human renal transplantation

that are currently clin. available or are under investigation in human trials. Clin. data are reviewed with respect to calcineurin inhibitor sparing regimens based on mycophenolate or sirolimus, the use of leflunomide and its derivative FK778, modulation of chemotaxis with FTY720 or chemokine receptor blockers and the results of costimulatory blockade. While selection of one of these strategies may allow a more individualized therapy, the immunosuppressive potential of each compound has to be weighed against adverse reactions for an individual patient.

IT 185915-33-7, FK778  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (new immunosuppressive strategies in renal transplant recipients)  
 RN 185915-33-7 HCAPLUS  
 CN 2-Hepten-6-ynamide, 2-cyano-3-hydroxy-N-[4-(trifluoromethyl)phenyl]- (9CI)  
 (CA INDEX NAME)

/ Structure 17 in file .gra /

REFERENCE COUNT: 89 THERE ARE 89 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2003:40163 HCAPLUS  
 DOCUMENT NUMBER: 138:83366  
 TITLE: Combination therapy for the treatment of immunological disorders  
 INVENTOR(S): Lindner, Juergen  
 PATENT ASSIGNEE(S): Aventis Behring G.m.b.H., Germany; Sanofi-Aventis Deutschland GmbH  
 SOURCE: Eur. Pat. Appl., 21 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1275638	A1	20030115	EP 2002-13275	20020618
EP 1275638	B1	20060614		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
DE 10132308	A1	20030130	DE 2001-10132308	20010706
AT 329898	E	20060715	AT 2002-13275	20020618
CA 2392187	AA	20030106	CA 2002-2392187	20020703
US 2003017166	A1	20030123	US 2002-189006	20020705
JP 2003063995	A2	20030305	JP 2002-196842	20020705
PRIORITY APPLN. INFO.:			DE 2001-10132308	A 20010706
OTHER SOURCE(S): MARPAT 138:83366				

AB The invention provides a combination treatment for excessive injurious immune reactions and degenerative processes, which contains (a) at least one undesired immune reaction- or degenerative process -participating antigen; (b) at least one protein synthesis inhibitor; and, if necessary, (c) an agent for suppressing an acute inflammatory reaction.

IT 185915-33-7  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (combination therapy for treatment of immunol. disorders)  
 RN 185915-33-7 HCAPLUS

10550099.trn

CN 2-Hepten-6-ynamide, 2-cyano-3-hydroxy-N-[4-(trifluoromethyl)phenyl]- (9CI)  
(CA INDEX NAME)

/ Structure 18 in file .gra /

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:373900 HCAPLUS

DOCUMENT NUMBER: 135:298435

TITLE: Leflunomide and its analogue X920715 synergize with  
cyclosporin A in preventing early graft failure and  
delaying graft rejection of xenogeneic islets in  
nonobese diabetic mice

AUTHOR(S): Gysemans, C.; Waer, M.; Laureys, J.; Bouillon, R.;  
Mathieu, C.

CORPORATE SOURCE: Department of Experimental Medicine and Endocrinology  
(LEGENDO), Catholic University of Leuven, Louvain,  
Belg.

SOURCE: Transplantation Proceedings (2001), 33(3), 2094-2095  
CODEN: TRPPA8; ISSN: 0041-1345

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Leflunomide (LEF) is a novel immunosuppressive drug that has already  
proven to be effective in interfering with both inflammation and tissue  
destruction. The capacity of LEF and its analog X920715, alone or in  
combination with cyclosporin A, in preventing early graft failure and  
prolonging graft survival of xenogeneic islets, was evaluated in  
spontaneously diabetic autoimmune nonobese diabetic (NOD) mice. Early  
graft failure following islet xenotransplantation in spontaneously  
diabetic NOD mice appeared to be an immune-mediated process  
because immunosuppressive manipulation of the host immune system can  
prevent this process. To determine the exact triggers of this  
phenomenon, further expts. are needed.

IT 185915-33-7

RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES  
(Uses)

(leflunomide and analog X920715 synergize with cyclosporin A in  
preventing early graft failure and delaying graft rejection of  
xenogeneic islets in nonobese diabetic mice)

RN 185915-33-7 HCAPLUS

CN 2-Hepten-6-ynamide, 2-cyano-3-hydroxy-N-[4-(trifluoromethyl)phenyl]- (9CI)  
(CA INDEX NAME)

/ Structure 19 in file .gra /

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:388358 HCAPLUS

DOCUMENT NUMBER: 131:29577

TITLE: Anion exchange HPLC for obtaining L-dihydroorotic acid  
and use thereof

INVENTOR(S): Milbert, Ulrike; Bartlett, Robert; Ruuth, Eric;

Fudali, Claude  
 PATENT ASSIGNEE(S): Hoechst Marion Roussel Deutschland GmbH, Germany  
 SOURCE: PCT Int. Appl., 33 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9930146	A1	19990617	WO 1998-EP7972	19981208
W: AU, BR, CA, CN, CZ, HU, ID, IN, JP, KR, MX, PL, RU, TR, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 933633	A1	19990804	EP 1997-121848	19971211
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2315326	AA	19990617	CA 1998-2315326	19981208
AU 9918775	A1	19990628	AU 1999-18775	19981208
AU 747993	B2	20020530		
EP 1036319	A1	20000920	EP 1998-963546	19981208
EP 1036319	B1	20050928		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
BR 9813559	A	20001010	BR 1998-13559	19981208
TR 200001671	T2	20001121	TR 2000-200001671	19981208
HU 200004510	A2	20010428	HU 2000-4510	19981208
JP 2001526387	T2	20011218	JP 2000-524655	19981208
RU 2228932	C2	20040520	RU 2000-118326	19981208
AT 305610	E	20051015	AT 1998-963546	19981208
ES 2248927	T3	20060316	ES 1998-963546	19981208
IN 193620	A	20040724	IN 2000-CN108	20000608
US 6545006	B1	20030408	US 2000-581142	20001211
HK 1033171	A1	20060728	HK 2001-103785	20010601
PRIORITY APPLN. INFO.:			EP 1997-121848	A 19971211
			WO 1998-EP7972	W 19981208

AB The invention relates to a process for obtaining L-dihydroorotic acid by chromatog. on an anionic exchange material in a base water mixture under a pressure from about 1.1 MPa to about 40 MPa. The process can be used to investigate the in vitro and in vivo activity of N-(4-trifluoromethylphenyl)-5-methylisoxazole-4-carboxamide, N-(4-trifluoromethylphenyl)-2-cyano-3-hydroxycrantonamide and similar compds. (dihydroorotic acid dehydrogenase inhibitors). The process can also be used to prepare a diagnostic assay.

IT 185915-33-7  
 RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
 (as L-dihydroorotic acid dehydrogenase inhibitor, determination or monitoring

of; anion exchange HPLC for obtaining L-dihydroorotic acid and use thereof)

RN 185915-33-7 HCAPLUS

CN 2-Hepten-6-ynamide, 2-cyano-3-hydroxy-N-[4-(trifluoromethyl)phenyl]- (9CI)  
 (CA INDEX NAME)

/ Structure 20 in file .gra /

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:178574 HCAPLUS

DOCUMENT NUMBER: 131:27608

TITLE: Derivatives of leflunomide's active metabolite A77-1726, the malononitrilamides (MNAs), prevent the development of experimental arthritis

AUTHOR(S): Schorlemmer, H. U.; Schleyerbach, R.

CORPORATE SOURCE: Research Laboratories Hoechst Marion Roussel Deutschland GmbH, Frankfurt, D-65926, Germany

SOURCE: International Journal of Immunotherapy (1998), 14(4), 177-184

CODEN: IJIMET; ISSN: 0255-9625

PUBLISHER: Bioscience Ediprint Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The novel disease-modifying antirheumatic drug (DMARD) leflunomide (ARAVA) recently has been shown to be safe and effective in the treatment of patients with active rheumatoid arthritis (RA), and has been approved by the Food and Drug Administration (FDA) for this indication.

Malononitrilamides (MNAs) belong to the derivs. of leflunomide's active metabolite A77-1726, and have been shown to be effective inhibitors of T- and B-cell-mediated autoimmune processes against a variety of models for autoimmune diseases. In the present study the authors investigated their antirheumatic activity in models of chronic degenerative joint disease of adjuvant arthritis (AA) in Lewis rats and spontaneously developing polyarthritis in MRL/lpr autoimmune mice.

Treatment of AA animals with various concns. of HMR-1279 or HMR-1715 (3-30 mg/kg) on days 1-19, given by oral gavage, prevented the disease from spreading to the noninjected extremity. The MNAs not only reduced the joint swelling, due to the disease progress, but also the degree of symptoms of AA, as indicated by the arthritis index. They demonstrated a significant and dose-dependent inhibition of arthritic paw edema, and reduced the arthritis index (95%). Autoimmune MRL/lpr mice spontaneously develop a disease very similar to human RA, especially considering the

articular

involvement such as swelling of the joints, pannus formation, proliferation of the synovial tissue, the presence of circulating rheumatoid factors (RF), and the development of autoantibodies against certain types of self-antigens, such as dsDNA or collagen type II, associated with massive lymph node enlargement and splenomegaly. Treating these autoimmune mice with the MNAs (20 mg/kg) by oral gavage from the 8th to the 12th week of their life resulted in an improved survival rate, which was largely due to inhibition of autoantibodies and RF. Also, a remarkable reduction of other Igs, such as IgG1 and IgE, could be found after treatment with HMR-1279 or HMR-1715. Clin. signs of polyarthritis (joint swelling), developing progressively with age in MRL/lpr mice, were reduced (65%) in treated animals. These results indicate that MNAs, like leflunomide and its active metabolite A77-1726, are effective in preventing the development of RA and rheumatoid systemic lupus erythematosus (SLE)-like disorders, and they may become a new effective generation of DMARDs for the treatment of human RA.

IT 185915-33-7, HMR-1715

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(derivs. of leflunomide's active metabolite A77-1726 malononitrilamides prevent development of exptl. arthritis)

RN 185915-33-7 HCAPLUS

CN 2-Hepten-6-ynamide, 2-cyano-3-hydroxy-N-[4-(trifluoromethyl)phenyl]- (9CI)



(CA INDEX NAME)

/ Structure 21 in file .gra /

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:147065 HCAPLUS

DOCUMENT NUMBER: 128:176183

TITLE: Use of xanthine derivatives for the modulation of  
apoptosis

INVENTOR(S): Muellner, Stefan; Dax, Claudia

PATENT ASSIGNEE(S): Hoechst A.-G., Germany

SOURCE: Eur. Pat. Appl., 17 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 821960	A1	19980204	EP 1997-112939	19970728
EP 821960	B1	20030409		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
DE 19640556	A1	19980402	DE 1996-19640556	19961001
US 5856330	A	19990105	US 1997-899023	19970723
AT 236637	E	20030415	AT 1997-112939	19970728
PT 821960	T	20030829	PT 1997-112939	19970728
ES 2191794	T3	20030916	ES 1997-112939	19970728
AU 9732367	A1	19980205	AU 1997-32367	19970729
AU 718237	B2	20000413		
CA 2212205	AA	19980131	CA 1997-2212205	19970730
JP 10067662	A2	19980310	JP 1997-204345	19970730
US 5981536	A	19991109	US 1998-175471	19981020
PRIORITY APPLN. INFO.:			DE 1996-19630837	A 19960731
			DE 1996-19640556	A 19961001
			US 1997-899023	A1 19970723

OTHER SOURCE(S): MARPAT 128:176183

GI

/ Structure 22 in file .gra /

AB Xanthine derivs. I [1 of R1, R3 = (CH<sub>2</sub>)<sub>n</sub>RCH<sub>3</sub>; if R = bond, n = 0-7; if R = CO or CR<sub>4</sub>(OH), n = 1-6; R<sub>4</sub> = H, C1-3 alkyl; other of R1, R3 = H, C1-7 alkyl, C4-8 cycloalkylalkyl, C2-6 oxaalkyl; R2 = C1-4 alkyl] are useful for modulation of abnormal apoptotic processes in various diseases such as autoimmune diseases, infarct, stroke, inflammation, neural degeneration, muscular atrophy or dystrophy, and cancer. I inhibit dephosphorylation of cofilin, a cytosolic 19-kDa actin-binding protein which is involved in transport of actin into the cell nucleus. Thus, 3-methyl-1-(5-oxohexyl)-7-propylxanthine was reacted with MeMgCl in THF, refluxed, and reacted with saturated aqueous NH<sub>4</sub>Cl solution to form 1-(5-hydroxy-5-methylhexyl)-3-methyl-7-propylxanthine (II). Activation of murine macrophages with Escherichia coli lipopolysaccharide (10 ng/mL)

resulted in 50% dephosphorylation of cofilin; dephosphorylation was reduced to 10% by simultaneous treatment of the cells with II (100  $\mu$ M). The effect of II (50  $\mu$ M) was potentiated by N-(4-trifluoromethylphenyl)-2-cyano-3-hydroxycrotonamide Na salt (10-20  $\mu$ M).

IT 185915-33-7

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(xanthine derivs. for modulation of apoptosis)

RN 185915-33-7 HCAPLUS

CN 2-Hepten-6-ynamide, 2-cyano-3-hydroxy-N-[4-(trifluoromethyl)phenyl]- (9CI)  
(CA INDEX NAME)

/ Structure 23 in file .gra /

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:147064 HCAPLUS

DOCUMENT NUMBER: 128:176182

TITLE: Use of isoxazole and crotonamide derivatives for the modulation of apoptosis

INVENTOR(S): Muellner, Stefan; Dax, Claudia

PATENT ASSIGNEE(S): Hoechst A.-G., Germany; Adventis Pharma GmbH

SOURCE: Eur. Pat. Appl., 11 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 821952	A1	19980204	EP 1997-112938	19970728
EP 821952	B1	20040331		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
DE 19640555	A1	19980402	DE 1996-19640555	19961001
US 6011051	A	20000104	US 1997-898756	19970723
AT 262901	E	20040415	AT 1997-112938	19970728
PT 821952	T	20040831	PT 1997-112938	19970728
ES 2218623	T3	20041116	ES 1997-112938	19970728
AU 9732368	A1	19980205	AU 1997-32368	19970729
AU 718728	B2	20000420		
CA 2212207	AA	19980131	CA 1997-2212207	19970730
JP 10087484	A2	19980407	JP 1997-204344	19970730

PRIORITY APPLN. INFO.: DE 1996-19630838 A 19960731  
DE 1996-19640555 A 19961001

OTHER SOURCE(S): MARPAT 128:176182

GI

/ Structure 24 in file .gra /

AB Isoxazole derivs. I [R1 = C1-4 alkyl, C3-5 cycloalkyl, C2-6 alkenyl, C2-6

alkynyl; R2 = CF3, OCF3, SCF3, OH, NO2, halo, Ph, (substituted) OPh, CH2Ph, CN; R3 = H, C1-4 alkyl, halo; X = N, CH] and crotonamide derivs. II (R1-R3, X as above) are useful for modulation of abnormal apoptotic processes in various diseases such as autoimmune diseases, infarct, stroke, inflammation, neural degeneration, muscular atrophy or dystrophy, and cancer. I and II inhibit dephosphorylation of cofilin, a cytosolic 19-kDa actin-binding protein which is involved in transport of actin into the cell nucleus. Thus, activation of murine macrophages with Escherichia coli lipopolysaccharide (10 ng/mL) resulted in 50% dephosphorylation of cofilin; dephosphorylation was completely inhibited by simultaneous treatment of the cells with N-(4-trifluoromethylphenyl)-2-cyano-3-hydroxycrotonamide Na salt (60 µM).

IT 185915-33-7

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(isoxazole and crotonamide derivs. for modulation of apoptosis)

RN 185915-33-7 HCAPLUS

CN 2-Hepten-6-ynamide, 2-cyano-3-hydroxy-N-[4-(trifluoromethyl)phenyl]- (9CI)  
(CA INDEX NAME)

/ Structure 25 in file .gra /

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 10 OF 10 HCAPLUS. COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:114395 HCAPLUS

DOCUMENT NUMBER: 128:239149

TITLE: The alloreactivity in the popliteal lymph node (PLN) assay is regulated by malononitrilamides (MNAs)

AUTHOR(S): Schorlemmer, H. U.; Ruuth, E.; Kurrle, R.

CORPORATE SOURCE: Research Laboratories Hoechst Marion Roussel (HMR), DG-Rheumatology/Immunology, c/o Behringwerke AG, Marburg, 35001, Germany

SOURCE: International Journal of Tissue Reactions (1997), 19(3/4), 157-161

CODEN: IJTEDP; ISSN: 0250-0868

PUBLISHER: Bioscience Ediprint Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Malononitrilamides (MNA 279 and MNA 715) represent a new class of low mol. weight immunosuppressants and belong to the derivs. of the primary metabolite of leflunomide A771726. They have been shown to prevent and reverse established acute allograft rejection and effectively prolong xenograft survival, and have also been found to be potent inhibitors of B- and T-cell mediated autoimmune processes. The MNAs mediate their effects by binding specifically to dehydro-orotate-dehydrogenase (DHODH) and inhibiting de novo pyrimidine biosynthesis, thereby blocking T- and B-cell proliferation and strongly suppressing the IgM and IgG antibody production. In this study we evaluated the effects of MNA 279 and MNA 715 on the in vivo lymphoproliferation that occurs after challenge with allogeneic cells in a local graft-vs.-host (GvH) reaction in Lewis + Brown-Norway (LBN) F1-hybrid rats by measuring the enlargement of the PLN draining the site of allogeneic cell injection. Oral administration of one of the two MNAs (7.5 to 50 mg/kg) on day 0 dose-dependently prevented the localized lymphoproliferative response and suppressed the lymph node hyperplasia. The MNAs even acted therapeutically when they were given during an ongoing alloreactivity as late as day 4 or 5 after challenge.

Consistent with the mode of action that MNAs inhibit de novo pyrimidine biosynthesis, a complete reversal of the immunosuppression on the lymphoproliferation in vivo was attempted in this protocol by addition of exogenous uridine during days 0 to 5. These data suggest that MNA 279 and MNA 715 mediate their antiproliferative and immunosuppressive effects in the PLN-assay in vivo by decreasing the activity of DHODH in the lymph node cells and thereby inhibiting pyrimidine biosynthesis.

IT 185915-33-7, MNA 715

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(alloreactivity in popliteal lymph node assay is regulated by malononitrilamides)

RN 185915-33-7 HCAPLUS

CN 2-Hepten-6-ynamide, 2-cyano-3-hydroxy-N-[4-(trifluoromethyl)phenyl]- (9CI)  
(CA INDEX NAME)

/ Structure 26 in file .gra /

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L16 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1004780 HCAPLUS

DOCUMENT NUMBER: 143:284722

TITLE: Anti-FK778 antibodies and highly sensitive immunoassay

INVENTOR(S): Tamura, Kouichi; Kato, Takeshi; Tabata, Kenji

PATENT ASSIGNEE(S): Astellas Pharma Inc., Japan

SOURCE: PCT Int. Appl., 45 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005085290	A1	20050915	WO 2005-JP3819	20050228
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2558596	AA	20050915	CA 2005-2558596	20050228
PRIORITY APPLN. INFO.:			AU 2004-901191	A 20040305
			WO 2005-JP3819	W 20050228

AB The authors disclose the preparation of haptens for the elicitation of antibodies capable of binding to FK778. In addition, the authors disclose a highly-sensitive immunoassay method, which utilizes an antibody to the FK778, and a test kit for measuring the concentration of FK778.

10550099.trn

IT 185915-33-7, FK778  
RL: ANT (Analyte); ANST (Analytical study)  
(anti-FK778 antibodies and immunoassay)  
RN 185915-33-7 HCAPLUS  
CN 2-Hepten-6-ynamide, 2-cyano-3-hydroxy-N-[4-(trifluoromethyl)phenyl]- (9CI)  
(CA INDEX NAME)

/ Structure 27 in file .gra /

IT 864378-19-8P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation of)  
RN 864378-19-8 HCAPLUS  
CN 2-Hepten-6-ynamide, 2-cyano-3,5-dihydroxy-N-[4-(trifluoromethyl)phenyl]-7-  
(trimethylsilyl)-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

/ Structure 28 in file .gra /

IT 864381-47-5P, FR 271764  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)  
RN 864381-47-5 HCAPLUS  
CN 2-Hepten-6-ynamide, 2-cyano-3,5-dihydroxy-N-[4-(trifluoromethyl)phenyl]-,  
(2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

/ Structure 29 in file .gra /

IT 6089-09-4, 4-Pentynoic acid  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction with cyanoacetylaminophenoxy hexanoate)  
RN 6089-09-4 HCAPLUS  
CN 4-Pentynoic acid (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

/ Structure 30 in file .gra /

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 2004:817854 HCAPLUS  
DOCUMENT NUMBER: 141:313895  
TITLE: Process for preparation of 2-cyano-3-hydroxy-hept-2-en-  
6-ynoic acid N-(4-trifluoromethylphenyl) amide  
INVENTOR(S): Omori, Hiroki; Kubota, Ariyoshi; Kawakami, Takeshi;  
Fujii, Yosuke; Matsumoto, Ikuo; Kitayama, Masato;  
Goto, Shunsuke; Hirabayashi, Satoshi  
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co. Ltd., Japan  
SOURCE: PCT Int. Appl., 49 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004085383	A1	<del>20041007</del>	WO 2004-JP3904	20040323
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
EP 1609778	A1	20051228	EP 2004-722662	20040323
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK			
US 2006217440	A1	20060928	US 2005-550099	20050921
PRIORITY APPLN. INFO.:			JP 2003-81335	A 20030324
			JP 2003-176706	A 20030620
			WO 2004-JP3904	W 20040323

OTHER SOURCE(S): CASREACT 141:313895

AB This invention pertains to a method for producing 2-cyano-3-hydroxy-hept-2-en-6-ynoic acid N-(4-trifluoromethylphenyl) amide, which comprises reacting 4-trifluoromethylaniline with 4-pentynoic acid in acetone in the presence of K<sub>2</sub>CO<sub>3</sub> and iso-Pr chlorocarbonate. A-, B-, and C-form crystals of the title compound were each selectively produced by recrystn. under the conditions of controlled recrystn. temperature and/or controlled recrystn. (precipitation) time. This invention provides a method to make the title compound in mild conditions without the production of industrial waste.

IT 185915-33-7P

RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)  
(preparation of 2-cyano-3-hydroxy-hept-2-en-6-ynoic acid N-(4-trifluoromethylphenyl) amide)

RN 185915-33-7 HCAPLUS

CN 2-Hepten-6-ynamide, 2-cyano-3-hydroxy-N-[4-(trifluoromethyl)phenyl]- (9CI)  
(CA INDEX NAME)

/ Structure 31 in file .gra /

IT 6089-09-4, 4-Pentynoic acid

RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation of 2-cyano-3-hydroxy-hept-2-en-6-ynoic acid N-(4-trifluoromethylphenyl) amide)

RN 6089-09-4 HCAPLUS

CN 4-Pentynoic acid (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

/ Structure 32 in file .gra /

REFERENCE COUNT:

7

THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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